

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

1. (Currently Amended) A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid based on adenovirus serotype, the vector system comprising:
  - (a) a first adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);
    - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
    - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;  
wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packing sequence;
  - (b) a second adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' adenovirus ITRs;
    - (ii) a second adenovirus serotype-specific cis-acting packaging sequence; and wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the second cis-acting packing sequence; ~~and~~
  - (c) an adenovirus replication competent host cell comprising a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence,  
  
wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence ~~a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.~~

2. (Previously Presented) The vector system of claim 1, wherein the adenovirus capsid and 52/55 kDa protein are from human adenovirus and wherein the first and second adenovirus nucleic acid sequences are from human adenovirus.

3. (Currently Amended) The vector system of claim 1, wherein the first and second adenovirus serotype-specific cis-acting packaging sequences are selected from the group consisting of adenovirus type 2 (Ad2), adenovirus type 5 (Ad5), adenovirus type 7 (Ad7), adenovirus type 12 (Ad12), adenovirus type 17 (Ad17), and adenovirus type 40 (Ad40) packaging sequences, and wherein the first serotype-specific cis-acting packaging sequence is from a different serotype than the second adenovirus serotype-specific cis-acting packaging sequence.

4. (Previously Presented) The vector system of claim 3, wherein the first adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 5 and the second adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 7.

5. (Previously Presented) The vector system of claim 3, wherein the first adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 7 and the second adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 5.

6-9. (Canceled)

10. (Previously Presented) The vector system of claim 1, wherein the failure to encode a functional 52/55 kDa trans-acting protein is due to a mutation in the sequence encoding the protein.

11. (Original) The vector system of claim 10, wherein the mutation is a missense mutation, a point mutation, a frameshift mutation or a deletion mutation.

12. (Canceled)

13. (Currently Amended) The vector system of claim 1, wherein the nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic acid sequence is encoded by a nucleic acid sequence functionally-associated with the genome of an adenovirus replication competent host cell containing the vector system.

14. (Original) The vector system of claim 13, wherein adenovirus replication competent host cell is a 293 cell line.

15-16. (Canceled)

17. (Currently Amended) A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid based on adenovirus serotype, the vector system comprising:

(a) a first adenovirus nucleic acid sequence comprising:

- (i) 5' and 3' adenovirus ITRs;
- (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
- (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;  
wherein the first adenovirus nucleic acid sequence comprises a defective or modified

adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packing sequence;

(b) a second adenovirus nucleic acid sequence comprising:

- (i) 5' and 3' adenovirus ITRs;
- (ii) a second adenovirus serotype-specific cis-acting packaging sequence; and
- (iii) a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein

that supports packaging of the first adenovirus nucleic acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence;

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence; and

(c) an adenovirus replication competent host cell;

wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence ~~a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.~~

18. (Canceled)

19. (Canceled)

20. (Previously Presented) A vector comprising a replication defective adenovirus sequence comprising:

- (a) a first adenovirus serotype-specific cis-acting packaging sequence; and
- (b) a nucleic acid sequence encoding a functional second adenovirus serotype-specific 52/55 kDa protein, wherein said protein is not specific for the first adenovirus serotype-specific cis-acting packaging sequence,

wherein the replication defective adenovirus sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

21. (Previously Presented) The vector of claim 20, further comprising at least one adenoviral nucleic acid sequence needed to produce an adenoviral capsid.

22. (Previously Presented) The vector of claim 21, further comprising sufficient adenoviral nucleic acid sequence to encode a complete adenoviral capsid when the vector is expressed in an adenovirus replication-competent host cell.

23. (Currently Amended) The vector of claim 20, wherein the first adenovirus serotype-specific cis-acting packaging sequence and second adenovirus serotype-specific ~~a nucleic acid~~ sequence are selected from the group consisting of adenovirus type 2 (Ad2), adenovirus type 5 (Ad5), adenovirus type 7 (Ad7), adenovirus type 12 (Ad12), adenovirus type 17 (Ad17), and adenovirus type 40 (Ad40), and wherein the first serotype-specific cis-acting packaging sequence is from a different serotype than the second adenovirus serotype-specific cis-acting packaging sequence.

24. (Previously Presented) The vector of claim 23, wherein the first adenovirus serotype sequence is adenovirus type 5 and the second adenovirus serotype sequence is adenovirus type 7.

25. (Previously Presented) The vector of claim 23, wherein the first adenovirus serotype sequence is adenovirus type 7 and the second adenovirus serotype sequence is adenovirus type 5.

26. (Currently Amended) A transformed or isolated infected cell comprising the vector ~~system of claim 1, claim 17, claim 18, claim 19 or the vector~~ of claim 20.

27. (Currently Amended) A kit useful for ~~making~~ producing adenovirus encapsidated replication defective nucleic acid sequences, the kit comprising: ~~one or more containers comprising the vector system of claim 1, claim 17, claim 18 or claim 19~~

(a) a container containing a first adenovirus nucleic acid sequence comprising:

(i) 5' and 3' adenovirus inverted terminal repeats (ITRs);

(ii) a first adenovirus serotype-specific cis-acting packaging sequence; and

(iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packing sequence;

(b) a container containing a second adenovirus nucleic acid sequence comprising:

(i) 5' and 3' adenovirus ITRs;

(ii) a second adenovirus serotype-specific cis-acting packaging sequence; and  
wherein the second adenovirus nucleic acid sequence complements the defective or  
modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton  
gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid  
sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans-  
acting protein specific for the second cis-acting packing sequence; and  
(c) a container containing an adenovirus replication competent host cell comprising a nucleic  
acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of  
the first adenovirus nucleic acid sequence and fails to support packaging of the second  
adenovirus nucleic acid sequence,  
wherein the replication defective adenovirus comprises the first adenovirus nucleic acid  
sequence.

28-30. (Canceled)

31. (Currently Amended) A method of producing a replication defective encapsidated adenovirus vector, comprising ~~the following steps~~:

(a) transforming or infecting into an adenovirus replication competent host cells

(i) a first adenovirus nucleic acid sequence comprising:

5' and 3' adenovirus inverted terminal repeats (ITRs);

a first adenovirus serotype-specific cis-acting packaging sequence; and

a heterologous gene operably linked to a transcriptional control sequence,

wherein the first adenovirus nucleic acid sequence comprises a defective or modified  
adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber  
gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to  
encode a 52/55 kDa trans-acting protein specific for the first cis-acting packing sequence;

(ii) a second adenovirus nucleic acid sequence comprising:

5' and 3' adenovirus ITRs;

a second adenovirus serotype-specific cis-acting packaging sequence,

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(iii) a nucleic acid sequence encoding an adenovirus 52/55 kDa protein specific for a first adenovirus serotype-specific cis-acting packaging sequence; and

(b) culturing the cells under conditions where the first ~~replication defective~~ adenovirus sequence is encapsidated to produce a replication defective adenovirus vector;

~~wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.~~

32. (Currently Amended) A method of producing a replication defective encapsidated adenovirus vector, comprising ~~the following steps~~:

(a) transforming or infecting into an adenovirus replication competent host cell a first and second adenovirus replication defective sequences, wherein the cell comprises a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of a first adenovirus nucleic acid sequence and fails to support packaging of a second adenovirus nucleic acid sequence, and wherein

(i) the first adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus inverted terminal repeats (ITRs);

a first adenovirus serotype-specific cis-acting packaging sequence; and

a heterologous gene operably linked to a transcriptional control sequence,

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packing sequence;

(ii) the second adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus ITRs;

a second adenovirus serotype-specific cis-acting packaging sequence,  
wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(b) culturing the cells under conditions where the first ~~replication defective~~ adenovirus sequence is encapsidated to produce a replication defective adenovirus vector;

~~wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.~~

33. (Currently Amended) A method of producing a replication defective encapsidated adenovirus vector, comprising the following steps:

(a) transforming or infecting a first and second adenovirus replication defective sequences into an adenovirus replication competent host cell, wherein

(i) the first adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus inverted terminal repeats (ITRs);

a first adenovirus serotype-specific cis-acting packaging sequence;

a heterologous gene operably linked to a transcriptional control sequence; and

a nucleic acid sequence encoding an adenovirus 52/55 kDa protein specific for the first adenovirus serotype-specific cis-acting packaging sequence,

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof; and

(ii) the second adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus ITRs;

a second adenovirus serotype-specific cis-acting packaging sequence,



wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(b) culturing the cells under conditions where the first ~~replication defective~~ adenovirus sequence is encapsidated to produce a replication defective adenovirus vector;

~~wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.~~

34. (Canceled)

35. (Previously Presented) A vector for selectively packaging replication defective nucleic acid sequences in adenovirus capsids, the vector comprising:

- (a) a replication defective adenovirus sequence comprising an adenovirus serotype 7 (Ad7) cis-acting packaging sequence;
- (b) a nucleic acid sequence encoding an adenovirus serotype 5 (Ad5) 52/55 kDa protein; and
- (c) an adenoviral nucleic acid sequence that encodes a viral capsid and fails to encode or produce an adenovirus 7 serotype 52/55 kDa trans-acting protein.

36-39. (Canceled)

40. (Currently Amended) A ~~packaging cell line~~ for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the cell ~~line~~ comprising:

- (a) a first adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);
  - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
  - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence,

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packaging sequence;

(b) a second adenovirus nucleic acid sequence comprising:

(i) 5' and 3' adenovirus ITRs;

(ii) a second adenovirus serotype-specific cis-acting packaging sequence,

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(c) a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein specific for the first adenovirus serotype-specific cis-acting packaging sequence,

wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence ~~a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.~~

41. (Currently Amended) A ~~packaging~~ cell line for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the cell line comprising:

~~(a) a nucleic acid sequence encoding an adenovirus serotype-specific 52/55 kDa trans-acting protein;~~

~~(b)~~ a first adenovirus nucleic acid sequence comprising:

(i) 5' and 3' adenovirus inverted terminal repeats (ITRs);

(ii) a first adenovirus serotype-specific cis-acting packaging sequence; and

(iii) a heterologous nucleic acid operably linked to a transcriptional control sequence,

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber

gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packaging sequence;

(e**b**) a second adenovirus nucleic acid sequence comprising:

- (i) 5' and 3' adenovirus ITRs;
- (ii) a second adenovirus serotype-specific cis-acting packaging sequence; ~~that fails to support the activity of the adenovirus serotype-specific 52/55 kDa trans-acting protein;~~
- (iii) a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence,

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, or a combination thereof of the first adenovirus nucleic acid sequence,

wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence ~~a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.~~

42. (Canceled)

43 (New) A kit useful for producing adenovirus encapsidated replication defective nucleic acid sequences, the kit comprising:

- (a) a first adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus ITRs;
  - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
  - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packaging sequence;

(b) a second adenovirus nucleic acid sequence comprising:

- (i) 5' and 3' adenovirus ITRs;

(ii) a second adenovirus serotype-specific cis-acting packaging sequence; and  
(iii) a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence;

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence; and

(c) an adenovirus replication competent host cell;

wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence.